

## Hit List

Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs
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Search Results - Record(s) 1 through 6 of 6 returned.

1. Document ID: US 20030150008 A1

**Using default format because multiple data bases are involved.**

L3: Entry 1 of 6

File: PGPB

Aug 7, 2003

PGPUB-DOCUMENT-NUMBER: 20030150008

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030150008 A1

TITLE: Transgenic plants containing altered levels of steroid compounds

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Karunanandaa, Balasulojini	St. Louis	MO	US	
Post-Beittemiller, Martha	St. Louis	MO	US	
Venkatramesh, Mylavarampu	St. Louis	MO	US	
Kishore, Ganesh M.	St. Louis	MO	US	
Thorne, Gregory M.	St. Louis	MO	US	
LeDeaux, John R.	St. Louis	MO	US	

US-CL-CURRENT: 800/278; 435/189, 435/410, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Drawn D
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2. Document ID: US 20030125573 A1

L3: Entry 2 of 6

File: PGPB

Jul 3, 2003

PGPUB-DOCUMENT-NUMBER: 20030125573

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030125573 A1

TITLE: Method of vitamin production

PUBLICATION-DATE: July 3, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Millis, James R.	Kohler	WI	US	

Saucy, Gabriel G.	Essex Fells	NY	US
Maurina-Brunker, Julie	Appleton	WI	US
McMullin, Thomas W.	Manitowoc	WI	US

US-CL-CURRENT: 549/411; 435/155

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw. De](#)

3. Document ID: US 20030092144 A1

L3: Entry 3 of 6

File: PGPB

May 15, 2003

PGPUB-DOCUMENT-NUMBER: 20030092144

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030092144 A1

TITLE: Production of farnesol and geranylgeraniol

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Millis, James R.	Kohler	WI	US	
Maurina-Brunker, Julie	Appleton	WI	US	
McMullin, Thomas W.	Manitowoc	WI	US	

US-CL-CURRENT: 435/157; 435/252.3

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Draw. De](#)

4. Document ID: US 20020108148 A1

L3: Entry 4 of 6

File: PGPB

Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020108148

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020108148 A1

TITLE: Nucleic acid sequences to proteins involved in isoprenoid synthesis

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boronat, Albert	Barcelona	MO	ES	
Campos, Narciso	Barcelona		ES	
Kishore, Ganesh M.	Creve Coeur		US	

US-CL-CURRENT: 800/284; 435/189, 435/320.1, 435/410, 435/69.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Drawn De
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5. Document ID: US 6531303 B1

L3: Entry 5 of 6

File: USPT

Mar 11, 2003

US-PAT-NO: 6531303

DOCUMENT-IDENTIFIER: US 6531303 B1

TITLE: Method of producing geranylgeraniol

DATE-ISSUED: March 11, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Millis; James R.	Kohler	WI		
Maurina-Brunker; Julie	Appleton	WI		
McMullin; Thomas W.	Manitowoc	WI		

US-CL-CURRENT: 435/155; 435/193, 435/254.21, 435/320.1, 435/441, 435/471

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Drawn De
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6. Document ID: US 6242227 B1

L3: Entry 6 of 6

File: USPT

Jun 5, 2001

US-PAT-NO: 6242227

DOCUMENT-IDENTIFIER: US 6242227 B1

TITLE: Method of vitamin production

DATE-ISSUED: June 5, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Millis; James R.	Kohler	WI		
Saucy; Gabriel G.	Essex Fells	NJ		
Maurina-Brunker; Julie	Appleton	WI		
McMullin; Thomas W.	Manitowoc	WI		
Hyatt; John A.	Kingsport	TN		

US-CL-CURRENT: 435/125

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Drawn De
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Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs	Generate OACS
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Terms	Documents
1-deoxy-D-xylulose 5 phosphate reductoisomerase.clm.	6

**Display Format:**

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L3: Entry 4 of 6

File: PGPB

Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020108148

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020108148 A1

TITLE: Nucleic acid sequences to proteins involved in isoprenoid synthesis

PUBLICATION-DATE: August 8, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boronat, Albert	Barcelona	MO	ES	
Campos, Narciso	Barcelona		ES	
Kishore, Ganesh M.	Creve Coeur		US	

US-CL-CURRENT: 800/284; 435/189, 435/320.1, 435/410, 435/69.1, 536/23.2

## CLAIMS:

What is claimed is:

1. An isolated nucleic acid sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase from a eukaryotic source.
2. An isolated nucleic acid sequence of claim 1, wherein said nucleic acid sequence is isolated from a plant source.
3. An isolated nucleic acid sequence of claim 2, wherein said nucleic acid sequence is isolated from *Arabidopsis*.
4. An isolated polynucleotide selected from the group consisting of: a) an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2; b) an isolated polynucleotide comprising SEQ ID NO:1; c) an isolated polynucleotide comprising a nucleotide sequence which has at least 70% identity to that of SEQ ID NO:1 over the entire length of SEQ ID NO:1; d) an isolated polynucleotide comprising a nucleotide sequence which has at least 80% identity to that of SEQ ID NO:1 over the entire length of SEQ ID NO:1; e) an isolated polynucleotide comprising a nucleotide sequence which has at least 90% identity to that of SEQ ID NO:1 over the entire length of SEQ ID NO:1; f) an isolated polynucleotide comprising a nucleotide sequence which has at least 95% identity to that of SEQ ID NO:1 over the entire length of SEQ ID NO:1; g) an isolated polynucleotide that hybridizes, under stringent conditions, to SEQ ID NO:1 or a fragment thereof; and h) an isolated polynucleotide complementary to the polynucleotide sequence of (a), (b), (c), (d), (e), (f), or (g).
5. A DNA construct, comprising; as operably associated components in the 5' to 3' direction of transcription, a promoter functional in a plant cell, a nucleic acid sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase, and a transcriptional termination sequence.

h e b b g e e e f c e

e ge

6. The DNA construct according to claim 5, wherein said nucleic acid sequence is isolated from a eukaryotic source.
7. The DNA construct according to claim 5, wherein said nucleic acid sequence is isolated from a plant source.
8. The DNA construct according to claim 5, wherein said nucleic acid sequence is isolated from Arabidopsis.
9. A host cell comprising the construct of claim 5.
10. A host cell according to claim 9, wherein the host cell is a plant cell.
11. A plant comprising a cell according to claim 10.
12. A method for the alteration of the isoprenoid content in a plant, comprising; transforming said host plant with a construct comprising as operably linked components, a transcriptional initiation region functional in a plant, a nucleic acid sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase, and a transcriptional termination region.
13. A method for the alteration of the isoprenoid content in a plant according to claim 12, wherein said nucleic acid sequence is in the sense orientation.
14. A method according to claim 13, wherein the isoprenoid content is increased.
15. A method for the alteration of the isoprenoid content in a plant according to claim 12, wherein said nucleic acid sequence is in the antisense orientation.
16. A method according to claim 15, wherein the isoprenoid content is decreased.
17. A method for producing an isoprenoid compound of interest in a plant cell, said method comprising obtaining a transformed plant, said plant having and expressing in its genome: a primary construct comprising a DNA sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase operably linked to a transcriptional initiation region functional in a plant cell; and, at least one secondary construct comprising a DNA sequence encoding a protein involved in the production of a particular isoprenoid operably linked to a transcriptional initiation region functional in a plant cell.
18. A method according to claim 17, wherein said protein is involved in the production of isoprenoids selected from the group consisting of tocopherols, carotenoids, monoterpenes, diterpenes, and plastoquinones.
19. A method for increasing the non-mevalonate isoprenoid biosynthetic flux in cell from a host plant, said method comprising transforming said host plant with a construct comprising as operably linked components, a transcriptional initiation region functional in a plant, a DNA coding 1-deoxy-D-xylulose 5-phosphate reductoisomerase, and a transcriptional termination region.
20. A method for modulating disease resistance in a plant, comprising: growing a plant which contains in its genome a construct which provides for expression of a 1-deoxy-D-xylulose 5-phosphate reductoisomerase gene.

## Hit List

**Clear** **Generate Collection** **Print** **Fwd Refs** **Bkwd Refs**  
**Generate OACS**

### Search Results - Record(s) 11 through 19 of 19 returned.

11. Document ID: US 20020108148 A1

L2: Entry 11 of 19

File: PGPB

Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020108148

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020108148 A1

TITLE: Nucleic acid sequences to proteins involved in isoprenoid synthesis

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boronat, Albert	Barcelona	MO	ES	
Campos, Narciso	Barcelona		ES	
Kishore, Ganesh M.	Creve Coeur		US	

US-CL-CURRENT: 800/284; 435/189, 435/320.1, 435/410, 435/69.1, 536/23.2

**Full** **Title** **Citation** **Front** **Review** **Classification** **Date** **Reference** **Sequences** **Attachments** **Claims** **KWIC** **Drawn** **De**

12. Document ID: US 20020069426 A1

L2: Entry 12 of 19

File: PGPB

Jun 6, 2002

PGPUB-DOCUMENT-NUMBER: 20020069426

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020069426 A1

TITLE: Methyl-D-erythritol phosphate pathway genes

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boronat, Albert	Barcelona	MO	ES	
Campos, Narciso	Barcelona	MO	ES	
Rodriguez-Concepcion, Manual	Barcelona	MO	ES	
Rohmer, Michel	Strasbourg		FR	
Seeman, Myriam	Rixheim		FR	

Valentin, Henry E.	Chesterfield	US
Venkatesh, Tyamagondlu V.	St. Louis	US
Venkatramesh, Mylavarampu	Ballwin	US

US-CL-CURRENT: 800/278; 435/69.8, 530/370, 536/23.6, 800/286

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn De](#)

13. Document ID: US 6531303 B1

L2: Entry 13 of 19

File: USPT

Mar 11, 2003

US-PAT-NO: 6531303

DOCUMENT-IDENTIFIER: US 6531303 B1

TITLE: Method of producing geranylgeraniol

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Millis; James R.	Kohler	WI		
Maurina-Bunker; Julie	Appleton	WI		
McMullin; Thomas W.	Manitowoc	WI		

US-CL-CURRENT: 435/155; 435/193, 435/254.21, 435/320.1, 435/441, 435/471

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn De](#)

14. Document ID: US 6420159 B2

L2: Entry 14 of 19

File: USPT

Jul 16, 2002

US-PAT-NO: 6420159

DOCUMENT-IDENTIFIER: US 6420159 B2

TITLE: 1-deoxy-D-xylulose-5-phosphate reductoisomerase, and methods of use

DATE-ISSUED: July 16, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Croteau; Rodney B.	Pullman	WA		
Lange; Bernd M.	Pullman	WA		

US-CL-CURRENT: 435/233

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn De](#)

15. Document ID: US 6387637 B1

L2: Entry 15 of 19

File: USPT

May 14, 2002

US-PAT-NO: 6387637

DOCUMENT-IDENTIFIER: US 6387637 B1

TITLE: Herbicide target genes and method

DATE-ISSUED: May 14, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Levin; Joshua Z.	Durham	NC		
Budziszewski; Gregory J.	Durham	NC		
Potter; Sharon L.	Raleigh	NC		
Wegrich; Lynette M.	San Jose	CA		

US-CL-CURRENT: 435/7.1; 530/350, 530/380

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Text	Claims	KWIC	Draw. De
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 16. Document ID: US 6281017 B1

L2: Entry 16 of 19

File: USPT

Aug 28, 2001

US-PAT-NO: 6281017

DOCUMENT-IDENTIFIER: US 6281017 B1

TITLE: 1-deoxy-d-xylulose-5-phosphate reductoisomerase and method of use

DATE-ISSUED: August 28, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Croteau; Rodney B.	Pullman	WA		
Lange; Bernd M.	Pullman	WA		

US-CL-CURRENT: 435/468; 435/189, 435/233, 435/320.1, 435/410, 435/476

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Text	Claims	KWIC	Draw. De
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 17. Document ID: US 6242227 B1

L2: Entry 17 of 19

File: USPT

Jun 5, 2001

US-PAT-NO: 6242227

DOCUMENT-IDENTIFIER: US 6242227 B1

TITLE: Method of vitamin production

DATE-ISSUED: June 5, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Millis; James R.	Kohler	WI		
Saucy; Gabriel G.	Essex Fells	NJ		
Maurina-Bunker; Julie	Appleton	WI		
McMullin; Thomas W.	Manitowoc	WI		
Hyatt; John A.	Kingsport	TN		

US-CL-CURRENT: 435/125

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Document](#) | [Abstract](#) | [Claims](#) | [KOMC](#) | [Drawn D](#)

18. Document ID: US 20020108148 A1

L2: Entry 18 of 19

File: DWPI

Aug 8, 2002

DERWENT-ACC-NO: 2003-066660

DERWENT-WEEK: 200306

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TITLE: New nucleic acid sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase from an eukaryotic source, useful for altering isoprenoid content and composition, and modulating disease resistance in plants

INVENTOR: BORONAT, A; CAMPOS, N ; KISHORE, G M

PRIORITY-DATA: 2001US-0987025 (November 13, 2001), 1999US-129899P (April 15, 1999), 1999US-146461P (July 30, 1999), 2000US-0549787 (April 14, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<u>US 20020108148 A1</u>	August 8, 2002		019	A01H005/00

INT-CL (IPC): A01 H 5/00; C07 H 21/04; C12 N 5/04; C12 N 9/02; C12 P 21/02

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Document](#) | [Abstract](#) | [Claims](#) | [KOMC](#) | [Drawn D](#)

19. Document ID: WO 200034448 A1, AU 200021633 A, EP 1135471 A1

L2: Entry 19 of 19

File: DWPI

Jun 15, 2000

DERWENT-ACC-NO: 2000-431295

DERWENT-WEEK: 200037

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TITLE: Novel polynucleotide encoding isopentenyl diphosphate biosynthetic enzymes useful for producing transgenic plants with altered isopentenyl diphosphate levels and for selecting polynucleotides affecting expression of the enzyme

INVENTOR: CAHOON, R E; LEE, J ; TAO, Y

PRIORITY-DATA: 1998US-110865P (December 4, 1998)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<u>WO 200034448 A1</u>	June 15, 2000	E	063	C12N009/04
<u>AU 200021633 A</u>	June 26, 2000		000	C12N009/04
<u>EP 1135471 A1</u>	September 26, 2001	E	000	C12N009/04

INT-CL (IPC): C12 N 9/04; C12 N 15/63; C12 N 15/67; C12 N 15/82; C12 N 15/86[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Cited by](#) | [Citing References](#) | [Claims](#) | [KWMC](#) | [Drawn](#) | [Des](#)[Clear](#) | [Generate Collection](#) | [Print](#) | [Fwd Refs](#) | [Bkwd Refs](#) | [Generate OACS](#)

Terms	Documents
1-deoxy-D-xylulose 5 phosphate reductoisomerase	19

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L2: Entry 16 of 19

File: USPT

Aug 28, 2001

US-PAT-NO: 6281017

DOCUMENT-IDENTIFIER: US 6281017 B1

TITLE: 1-deoxy-d-xylulose-5-phosphate reductoisomerase and method of use

DATE-ISSUED: August 28, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Croteau; Rodney B.	Pullman	WA		
Lange; Bernd M.	Pullman	WA		

US-CL-CURRENT: 435/468; 435/189, 435/233, 435/320.1, 435/410, 435/476

## CLAIMS:

What is claimed is:

1. An isolated nucleic acid molecule that hybridizes under stringent conditions to the nucleic acid molecule of SEQ ID NO:1, or to the complement of the nucleic acid molecule of SEQ ID NO:1, provided that said isolated nucleic acid molecule does not consist of a nucleic acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:11 or a nucleic acid sequence complementary to a nucleic acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:11, wherein said stringent hybridization conditions consist of hybridization in 3.times.SSC at 65.degree. C. for 16 hours, followed by two washes in 2.times.SSC at 23.degree. C. for 20 minutes per wash, followed by one wash in 0.5.times.SSC at 55.degree. C. for 30 minutes.
2. An isolated nucleic acid molecule of claim 1 wherein said isolated nucleic acid molecule encodes a plant 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein.
3. An isolated nucleic acid molecule of claim 1 wherein said isolated nucleic acid molecule encodes an essential oil plant 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein.
4. An isolated nucleic acid molecule of claim 3 wherein said isolated nucleic acid molecule encodes a *Mentha* 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein.
5. An isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule encodes a 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein comprising the amino acid sequence set forth in SEQ ID NO:2.
6. An isolated nucleic acid molecule of claim 1 comprising the nucleic acid sequence of SEQ ID NO:1.

7. A replicable vector comprising a first nucleic acid molecule that hybridizes under stringent conditions to a second nucleic acid molecule consisting of the nucleic acid sequence set forth in SEQ ID NO:1, or to a third nucleic acid molecule consisting of the complement of the nucleic acid sequence set forth in SEQ ID NO:1, provided that said first nucleic acid molecule does not consist of a nucleic acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:11 or a nucleic acid sequence complementary to a nucleic acid sequence selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:11, wherein said stringent hybridization conditions consist of hybridization in 3.times.SSC at 65.degree. C. for 16 hours, followed by two washes in 2.times.SSC at 23.degree. C. for 20 minutes per wash, followed by one wash in 0.5.times.SSC at 55.degree. C. for 30 minutes.

8. A replicable vector of claim 7 wherein said first nucleic acid molecule encodes a plant 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein.

9. A replicable vector of claim 7 wherein said first nucleic acid molecule encodes a *Mentha* 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein.

10. A replicable vector of claim 7 wherein said first nucleic acid molecule encodes a 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein comprising the amino acid sequence set forth in SEQ ID NO:2.

11. A replicable vector of claim 7 wherein said first nucleic acid molecule comprises the nucleic acid sequence set forth in SEQ ID NO:1, or the complement of the nucleic acid sequence set forth in SEQ ID NO:1.

12. A host cell comprising a vector of claim 7.

13. A host cell comprising a vector of claim 11.

14. A host cell of claim 12 wherein said host cell is a plant cell.

15. A host cell of claim 13 wherein said host cell is a plant cell.

16. A method of enhancing the level of expression of 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein in a host cell comprising introducing into said host cell a replicable expression vector comprising a nucleic acid molecule that encodes a 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein under conditions that enable expression of said protein in said host cell, wherein said nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of the nucleic acid sequence set forth in SEQ ID NO:1 under hybridization conditions consisting of hybridization in 3.times.SSC at 65.degree. C. for 16 hours, followed by two washes in 2.times.SSC at 23.degree. C. for 20 minutes per wash, followed by one wash in 0.5.times.SSC at 55.degree. C. for 30 minutes.

17. A method of reducing the level of expression of 1-deoxy-D-xylulose-5-phosphate reductoisomerase protein in a host cell comprising introducing into said host cell a replicable expression vector comprising a nucleic acid molecule that expresses an RNA molecule that hybridizes under stringent conditions to the nucleic acid sequence of SEQ ID NO:1, wherein said stringent hybridization conditions consist of hybridization in 3.times.SSC at 65.degree. C. for 16 hours, followed by two washes in 2.times.SSC at 23.degree. C. for 20 minutes per wash, followed

by one wash in 0.5.times.SSC at 55.degree. C. for 30 minutes.

## WEST Search History

DATE: Tuesday, January 13, 2004

**Hide? Set Name Query** **Hit Count**

*DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ*

<input type="checkbox"/>	L3	1-deoxy-D-xylulose 5 phosphate reductoisomerase.clm.	6
<input type="checkbox"/>	L2	1-deoxy-D-xylulose 5 phosphate reductoisomerase	19

*DB=USPT; PLUR=YES; OP=ADJ*

<input type="checkbox"/>	L1	6465225	1
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END OF SEARCH HISTORY

=> file medline caplus biosis embase biotechds scisearch  
COST IN U.S. DOLLARS SINCE FILE  
ENTRY  
FULL ESTIMATED COST 0.42

FILE 'MEDLINE' ENTERED AT 11:33:02 ON 13 JAN 2004

FILE 'CAPLUS' ENTERED AT 11:33:02 ON 13 JAN 2004  
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FILE 'SCISEARCH' ENTERED AT 11:33:02 ON 13 JAN 2004  
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=> 1-deoxy-D-xylulose 5 phosphate reductoisomerase  
1-DEOXY-D-XYLULOSE IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s 1-deoxy-D-xylulose 5 phosphate reductoisomerase  
[1] 297 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE

=> s 11 and isoprenoid  
L2 162 L1 AND ISOPRENOID

=> s 12 and (dna or nucleic acid or rna)  
2 FILES SEARCHED

HS 26 EZ FIND (DNA OR NUCLEIC ACID) 11

L4 12 L3 AND 2-C METHYL-D-ERYTHRITOL 4-PHOSPHATE

=> dup rem 14  
PROCESSING COMPLETED FOR L4  
L5 10 DUP REM L4 (2 DUPLICATES REMOVED)

• 15 and 1880-1888/pw

=> 15 and 1990 1998, by  
L5 IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

```
=> s 15 and 1990-1998/py
      4 FILES SEARCHED...
L6          1 L5 AND 1990-1998/PY
```

=> d 16 ibib ab

L6 ANSWER 1 OF 1 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 1998305569 EMBASE  
TITLE: A 1-deoxy-D-xylulose  
5-phosphate reductoisomerase  
catalyzing the formation of 2-C-

Searches  
Updated  
1/13/04

**methyl-D-erythritol 4**  
-phosphate in an alternative nonmevalonate pathway for terpenoid biosynthesis.  
AUTHOR: Takahashi S.; Kuzuyama T.; Watanabe H.; Seto H.  
CORPORATE SOURCE: H. Seto, Inst. of Molec./Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo 113-0032, Japan.  
c00402@simail.nc.jp

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (18 Aug 1998) 95/17 (9879-9884).

Refs: 38  
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology  
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Several eubacteria including *Escherichia coli* use an alternative nonmevalonate pathway for the biosynthesis of isopentenyl diphosphate instead of the ubiquitous mevalonate pathway. In the alternative pathway, 2-C- methyl-D-erythritol or its 4-phosphate, which is proposed to be formed from 1-deoxy-D-xylulose 5-phosphate via intramolecular rearrangement followed by reduction process, is one of the biosynthetic precursors of isopentenyl diphosphate. To clone the gene(s) responsible for synthesis of **2-C-methyl-D-erythritol 4-phosphate**, we prepared and selected *E. coli* mutants with an obligatory requirement for 2-C-methylerythritol for growth and survival. All the **DNA** fragments that complemented the defect in synthesizing **2-C-methyl-D- erythritol 4-phosphate** of these mutants contained the *yaeM* gene, which is located at 4.2 min on the chromosomal map of *E. coli*. The gene product showed significant homologies to hypothetical proteins with unknown functions present in *Haemophilus influenzae*, *Synechocystis* sp. PCC6803, *Mycobacterium tuberculosis*, *Helicobacter pylori*, and *Bacillus subtilis*. The purified recombinant *yaeM* gene product was overexpressed in *E. coli* and found to catalyze the formation of **2-C-methyl-D-erythritol 4-phosphate** from 1-deoxy- D-xylulose 5-phosphate in the presence of NADPH. Replacement of NADPH with NADH decreased the reaction rate to about 1% of the original rate. The enzyme required Mn<sup>2+</sup>, Co<sup>2+</sup>, or Mg<sup>2+</sup> as well. These data clearly show that the *yaeM* gene encodes an enzyme, designated **1-deoxy-D-xylulose 5-phosphate reductoisomerase**, that synthesizes **2-C-methyl-D-erythritol 4-phosphate** from 1-deoxy-D-xylulose 5-phosphate, in a single step by intramolecular rearrangement and reduction and that this gene is responsible for terpenoid biosynthesis in *E. coli*.

=> d his

(FILE 'HOME' ENTERED AT 11:32:03 ON 13 JAN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHDS, SCISEARCH' ENTERED AT 11:33:02 ON 13 JAN 2004

L1 297 S 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE  
L2 162 S L1 AND ISOPRENOID  
L3 26 S L2 AND (DNA OR NUCLEIC ACID OR RNA)  
L4 12 S L3 AND 2-C METHYL-D-ERYTHRITOL 4-PHOSPHATE  
L5 10 DUP REM L4 (2 DUPLICATES REMOVED)  
L6 1 S L5 AND 1990-1998/PY

=> d 15 1-10 ibib ab

L5 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:123201 CAPLUS  
 DOCUMENT NUMBER: 136:162385  
 TITLE: Methyl-D-erythritol phosphate pathway gene *gcpE* from  
*Arabidopsis thaliana* and other plants  
 INVENTOR(S): Boronat, Albert; Campos, Narciso; Rodriguez-  
 Concepcion, Manuel; Rohmer, Michel; Seeman, Myriam;  
 Valentin, Henry E.; Venkatesh, Tyamagondlu V.;  
 Venkatramesh, Mylavarampu  
 PATENT ASSIGNEE(S): Monsanto Technology, LLC, USA  
 SOURCE: PCT Int. Appl., 155 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012478	A2	20020214	WO 2001-US24335	20010806
WO 2002012478	C1	20020704		
WO 2002012478	A3	20030703		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090522	A5	20020218	AU 2001-90522	20010806
US 2002069426	A1	20020606	US 2001-921992	20010806
EP 1356033	A2	20031029	EP 2001-970529	20010806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.: US 2000-223483P P 20000807 WO 2001-US24335 W 20010806				

AB The present invention provides and includes nucleic acids, proteins and antibodies assocd. with novel genes in the methyl-D-erythritol phosphate (MEP) biosynthesis pathway. Specifically, a homolog of the *Escherichia coli* *gcpE* gene is found in *Arabidopsis thaliana* which catalyzes the conversion of 2-C-methyl-D-erythritol 2,4-cyclodiphosphate to (E)-1-(4-hydroxy-3-methylbut-2-enyl) diphosphate. Partial gene sequences are also provided from soybean, tomato, *Mesembryanthemum crystallinum*, rice, maize, loblolly pine, soybean, *Brassica*, and *Physcomitrella patens*. The invention further encompasses methods utilizing such mols., for example in gene isolation, gene anal. and the prodn. of transgenic plants. The present invention also includes transgenic plants modified to express proteins assocd. with the MEP pathway. Modulation of **isoprenoid**, tocopherol, monoterpane, and carotenoid levels can be achieved in transgenic plants.

L5 ANSWER 2 OF 10 MEDLINE on STN  
 ACCESSION NUMBER: 2001489332 MEDLINE  
 DOCUMENT NUMBER: 21425086 PubMed ID: 11532167  
 TITLE: **1-Deoxy-D-xylulose 5-phosphate reductoisomerase**  
 and plastid **isoprenoid** biosynthesis during tomato  
 fruit ripening.  
 AUTHOR: Rodriguez-Concepcion M; Ahumada I; Diez-Juez E;  
 Sauret-Gueto S; Lois L M; Gallego F; Carretero-Paulet L;  
 Campos N; Boronat A  
 CORPORATE SOURCE: Departament de Bioquimica i Biologia Molecular, Facultat de  
 Quimica, Universitat de Barcelona, Marti i Franques 1-7,

SOURCE: 08028 Barcelona, Spain.. mrodrigu@sun.bq.ub.es  
PLANT JOURNAL, (2001 Aug) 27 (3) 213-22.  
Journal code: 9207397. ISSN: 0960-7412.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AF331705  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20010905  
Last Updated on STN: 20020122  
Entered Medline: 20011204

AB The recently discovered **2-C-methyl-D-erythritol 4-phosphate** (MEP) pathway for the biosynthesis of plastid isoprenoids (including carotenoids) is not fully elucidated yet despite its central importance for plant life. It is known, however, that the first reaction completely specific to the pathway is the conversion of 1-deoxy-D-xylulose 5-phosphate (DXP) into MEP by the enzyme DXP reductoisomerase (DXR). We have identified a tomato cDNA encoding a protein with homology to DXR and in vivo activity, and show that the levels of the corresponding DXR mRNA and encoded protein in fruit tissues are similar before and during the massive accumulation of carotenoids characteristic of fruit ripening. The results are consistent with a non-limiting role of DXR, and support previous work proposing DXP synthase (DXS) as the first regulatory enzyme for plastid **isoprenoid** biosynthesis in tomato fruit. Inhibition of DXR activity by fosmidomycin showed that plastid **isoprenoid** biosynthesis is required for tomato fruit carotenogenesis but not for other ripening processes. In addition, dormancy was reduced in seeds from fosmidomycin-treated fruit but not in seeds from the tomato yellow ripe mutant (defective in phytoene synthase-1, PSY1), suggesting that the isoform PSY2 might channel the production of carotenoids for abscisic acid biosynthesis. Furthermore, the complete arrest of tomato seedling development using fosmidomycin confirms a key role of the MEP pathway in plant development.

L5 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:832956 CAPLUS  
DOCUMENT NUMBER: 137:16268  
TITLE: First-time isolation of an isoprene synthase gene and heterologous expression of a gene originating from poplar and characterization of entry genes of a mevalonate-independent **isoprenoid** biosynthesis path from the cyanobacterium *Synechococcus leopoliensis*  
AUTHOR(S): Miller, Barbara  
CORPORATE SOURCE: Germany  
SOURCE: Schriftenreihe des Fraunhofer-Instituts Atmosphaerische Umweltforschung (2001), 68, a,b,c,d,e,f,i-v,1-145  
CODEN: SFAUFS; ISSN: 1436-1094  
PUBLISHER: Shaker Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: German  
AB The occurrence of **2-C-methyl-D-erythritol-4-phosphate** (MEP) metab. was evidenced in cyanobacteria. A cosmid gene bank of *Synechococcus leopoliensis* contg. 1384 clones was provided. The genes encoding deoxyxylulosephosphate (DXP) synthase (DXS) and DXP reductoisomerase (DXR) were localized. Open reading frames of the dxs and dxr operons were identified, cloned, and expressed in *Escherichia coli*. The overexpression resulted in an 8-fold increase of the content of dimethylallyl diphosphate. The functionality of DXR was evidenced by photometric detn. of the NADPH oxidn. dependent on DXP. An isoprene synthase gene was isolated from a .lambda.-gene bank of the plant hybrid *Populus alba* x P.

tremula. High homologies to monoterpene synthases were found by sequencing. Overexpression of the isoprene synthase gene contg. an N-terminal signal peptide caused a 100-fold increase in isoprene formation. Simultaneous overexpression of the dxs gene of *S. leopoliensis* addnl. increased isoprene formation fourfold. Recombinant isoprene synthase increased the isoprene formation 200-fold in comparison with the limonene formation dependent on geranylphosphate.

REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:158099 CAPLUS  
DOCUMENT NUMBER: 134:291006  
TITLE: Investigation of a novel biosynthetic pathway to isopentenyl diphosphate in *Escherichia coli* and *Zymomonas mobilis*: Identification and characterization of involved genes  
AUTHOR(S): Grolle, Sigrid  
CORPORATE SOURCE: Germany  
SOURCE: Berichte des Forschungszentrums Juelich (2000), Juel-3799, i-ix, 1-111  
CODEN: FJBEE5; ISSN: 0366-0885  
DOCUMENT TYPE: Report  
LANGUAGE: German  
AB In the last few years, evidence has emerged that in bacteria a novel biosynthetic pathway to isopentenyl diphosphate exists. In this pathway isopentenyl diphosphate is formed from pyruvate and glyceraldehyde 3-phosphate. In the 1st reaction step these C3 compds. are combined to 1-deoxyxylulose 5-phosphate whereby pyruvate is decarboxylated. The gene encoding the 1-deoxyxylulose 5-phosphate synthase was identified in *E. coli* by searching for transketolase-homologous genes. The corresponding gene product was purified and was shown by NMR anal. to catalyze in a thiamin diphosphate (TPP) and Mg<sup>2+</sup> dependent reaction the synthesis of 1-deoxyxylulose 5-phosphate. Phylogenetic investigation revealed that the 1-deoxyxylulose 5-phosphate synthase belongs to a new family of TPP dependent enzymes. The dxs gene is located at 9 min on the *E. coli* chromosome and is organized in 1 operon with a putative aldonoketo-reductase gene. The disruption of this *E. coli* gene yielded no phenotype which indicates that the gene is not involved in the novel pathway. The gene encoding the second enzyme of the pathway, the 1-deoxyxylulose 5-phosphate reductoisomerase, was isolated from *Z. mobilis*. The 1-deoxyxylulose 5-phosphate reductoisomerase catalyzes the NADPH and Mn<sup>2+</sup> dependent rearrangement and subsequent redn. of 1-deoxyxylulose 5-phosphate to 2C-methylerythritol 4-phosphate. The enzyme activity is competitively inhibited by the antibiotic fosmidomycin with a Ki of 0,6 .mu.M. By a *E. coli* strain engineered to produce the **isoprenoid** zeaxanthin the gene encoding IPP-isomerase, but no further genes of the novel pathway could be isolated from an *E. coli* expression gene library.

REFERENCE COUNT: 236 THERE ARE 236 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2000:34841 CAPLUS  
DOCUMENT NUMBER: 132:89232  
TITLE: Vitamin production by fermentative biosynthesis of intermediates using genetically engineered microorganisms followed by chemical synthesis  
INVENTOR(S): Millis, James R.; Saucy, Gabriel G.; Maurina-Brunker, Julie; McMullin, Thomas W.  
PATENT ASSIGNEE(S): DCV, Inc., USA  
SOURCE: PCT Int. Appl., 239 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001650	A1	20000113	WO 1999-US15264	19990706
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948630	A1	20000124	AU 1999-48630	19990706
EP 1095002	A1	20010502	EP 1999-932295	19990706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6410755	B1	20020625	US 1999-348097	19990706
JP 2002519049	T2	20020702	JP 2000-558056	19990706
US 6531303	B1	20030311	US 1999-350275	19990706
US 2003125573	A1	20030703	US 2001-902187	20010709
US 2003092144	A1	20030515	US 2001-909558	20010720
PRIORITY APPLN. INFO.:			US 1998-91951P	P 19980706
			US 1998-91964P	P 19980706
			US 1998-91983P	P 19980706
			US 1998-91868P	P 19980706
			US 1999-348097	A1 19990706
			US 1999-350275	A1 19990706
			WO 1999-US15264	W 19990706

OTHER SOURCE(S): MARPAT 132:89232

AB The invention provides methods of producing vitamin E (.alpha.-tocopherol and .alpha.-tocopheryl esters), vitamin A (retinol), or .beta.-carotene. The methods comprise using a biol. system to produce farnesol or geranylgeraniol. Biosynthesis of the farnesol or geranylgeraniol intermediates is enhanced by shifting microbial metab. away from sterol biosynthesis via genetic inactivation of the squalene synthase ERG9 gene or by inactivation of squalene synthase by zaragozic acid in a strain with a functional ERG9 gene. Geranylgeraniol biosynthesis is further enhanced in strains over-expressing any of 4 different cloned geranylgeranyl pyrophosphate synthase genes: (1) BTS1 gene from *Saccharomyces cerevisiae*; (2) crtE gene from *Erwinia uredovora*; (3) a1-3 gene from *Neurospora crassa*; or (4) ggs gene from *Gibberella fujikuroi*. Overexpressing of hydroxymethyl-CoA reductase and/or the ERG20 gene which encodes farnesyl pyrophosphate synthase in *Saccharomyces cerevisiae* also enhances biosynthesis of fermentative intermediates. Finally, over-expression of multiple **isoprenoid** pathway genes or alternative pathway (Rohmer pathway) was further investigated in strains that have an erg9 mutation and elevated levels of hydroxymethylglutaryl-CoA reductase. The farnesol or geranylgeraniol fermn. products are then chem. converted into .alpha.-tocopherol, an .alpha.-tocopheryl ester, vitamin A, or .beta. carotene.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2000:516559 SCISEARCH

THE GENUINE ARTICLE: 330AU

TITLE: Characterization of 1-Deoxy-D

-xylulose 5-phosphate

reductoisomerase, an enzyme involved in isopentenyl diphosphate biosynthesis, and identification of its catalytic amino acid residues

AUTHOR: Kuzuyama T; Takahashi S; Takagi M; Seto H (Reprint)  
CORPORATE SOURCE: UNIV TOKYO, INST MOL & CELLULAR BIOSCI, BUNKYO KU, TOKYO  
1130032, JAPAN (Reprint); UNIV TOKYO, INST MOL & CELLULAR  
BIOSCI, BUNKYO KU, TOKYO 1130032, JAPAN  
COUNTRY OF AUTHOR: JAPAN  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (30 JUN 2000) Vol. 275,  
No. 26, pp. 19928-19932.  
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC,  
9650 ROCKVILLE PIKE, BETHESDA, MD 20814.  
ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 26

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB 1-Deoxy-D-xylulose 5-phosphate (DXP) reductoisomerase, which simultaneously catalyzes the intramolecular rearrangement and reduction of DXP to form **2-C-methyl-D-erythritol 4-phosphate**, constitutes a key enzyme of an alternative mevalonate-independent pathway for isopentenyl diphosphate biosynthesis. The dxr gene encoding this enzyme from *Escherichia coli* was overexpressed as a histidine-tagged protein and characterized in detail. DNA sequencing analysis of the dxr genes from 10 *E. coli* dxr-deficient mutants revealed base substitution mutations at four points: two nonsense mutations and two amino acid substitutions (Gly(14) to Asp(14) and Glu(231) to Lys(231)). Diethyl pyrocarbonate treatment inactivated DXP reductoisomerase, and subsequent hydroxylamine treatment restored the activity of the diethyl pyrocarbonate-treated enzyme. To characterize these defects, we overexpressed the mutant enzymes G14D, E231K, H153Q, H209Q, and H257Q. All of these mutant enzymes except for G14D were obtained as soluble proteins. Although the purified enzyme E231K had wildtype K-m values for DXP and NADPH, the mutant enzyme had less than a 0.24% wild-type k(cat) value. K-m values of H153Q, H209Q, and H257Q for DXP increased to 3.5-, 7.6-, and 19-fold the wild-type value, respectively. These results indicate that Glu(231) of *E. coli* DXP reductoisomerase plays an important role(s) in the conversion of DXP to **2-C-methyl-D-erythritol 4-phosphate**, and that His(153), His(209), and His(257), in part, associate with DXP binding in the enzyme molecule.

L5 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:140254 CAPLUS  
DOCUMENT NUMBER: 132:275501  
TITLE: Overlooked nonmevalonate pathway for isopentenyl diphosphate biosynthesis and specific inhibitors  
AUTHOR(S): Kuzuyama, Tomohisa; Seto, Haruo  
CORPORATE SOURCE: Institute of Molecular and Cellular Biosciences, University of Tokyo, Tokyo, 113-0032, Japan  
SOURCE: Nihon Yukagakkaishi (2000), 49(2), 119-125  
CODEN: NIYUFC; ISSN: 1341-8327  
PUBLISHER: Nihon Yukagaku Gakkai  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review with 19 refs. Several eubacteria including *Escherichia coli* utilize a mevalonate-independent pathway (nonmevalonate pathway) for the biosynthesis of isopentenyl diphosphate. In the nonmevalonate pathway, **2-C-methyl-D-erythritol** or its **4-phosphate**, possibly formed from **1-deoxy-D-xylulose 5-phosphate (DXP)** via intramol. rearrangement followed by redn., is a biosynthetic precursors of isopentenyl diphosphate. To clone the gene(s) responsible for the synthesis of **2-C-methyl-D-erythritol 4-phosphate (MEP)**, *E. coli* mutants with obligatory requirement for **2-C-methylerythritol** for growth and survival were prep'd. DNA fragments complementing the defect in synthesizing MEP of these mutants

contained the *yaeM* gene located at 4.2 min on the chromosomal map of *E. coli*. The gene product showed significant homol. to hypothetical proteins with unknown functions in many eubacteria. The *yaeM* gene product overexpressed in *E. coli* was found to catalyze the formation of MEP from DXP in the presence of NADPH. The *yaeM* gene is thus clearly shown to encode a novel enzyme, DXP reductoisomerase, which synthesizes MEP from DXP in a single step by intramol. rearrangement and redn. Fosmidomycin was noted to be a specific inhibitor of DXP reductoisomerase.

L5 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 1  
ACCESSION NUMBER: 1999:247659 BIOSIS  
DOCUMENT NUMBER: PREV199900247659  
TITLE: **Isoprenoid biosynthesis via a mevalonate-independent pathway in plants: Cloning and heterologous expression of 1-deoxy-D-xylulose-5-phosphate reductoisomerase from peppermint.**  
AUTHOR(S): Lange, B. Markus; Croteau, Rodney [Reprint author]  
CORPORATE SOURCE: Department of Biochemistry and Biophysics, Institute of Biological Chemistry, Washington State University, Pullman, WA, 99164-6340, USA  
SOURCE: Archives of Biochemistry and Biophysics, (May 1, 1999) Vol. 365, No. 1, pp. 170-174. print.  
CODEN: ABBIA4. ISSN: 0003-9861.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Jul 1999  
Last Updated on STN: 2 Jul 1999

AB Two distinct pathways are utilized by plants for the biosynthesis of isopentenyl diphosphate, the universal precursor of isoprenoids. The classical acetate/mevalonate pathway operates in the cytosol, whereas plastidial isoprenoids originate via a novel mevalonate-independent route that involves a transketolase-catalyzed condensation of pyruvate and D-glyceraldehyde-3-phosphate to yield 1-deoxy-D-xylulose-5-phosphate as the first intermediate. Based on in vivo feeding experiments, rearrangement and reduction of deoxxyxylulose phosphate have been proposed to give rise to **2-C-methyl-D-erythritol-4-phosphate** as the second intermediate of this pyruvate/glyceraldehyde-3-phosphate pathway (1-3). The cloning of an *Escherichia coli* gene encoding an enzyme capable of converting 1-deoxy-D-xylulose-5-phosphate to 2-C-erythritol-4-phosphate was recently reported (4). A cloning strategy was developed for isolating the gene encoding a plant homolog of this enzyme from peppermint (*Mentha x piperita*), and the identity of the resulting cDNA was confirmed by heterologous expression in *E. coli*. Unlike the microbial reductoisomerase, the plant ortholog encodes a preprotein bearing an N-terminal plastidial transit peptide that directs the enzyme to plastids where the mevalonate-independent pathway operates in plants. The peppermint gene comprises an open reading frame of 1425 nucleotides which, when the plastidial targeting sequence is excluded, encodes a deduced enzyme of approximately 400 amino acid residues with a mature size of about 43.5 kDa.

L5 ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN  
ACCESSION NUMBER: 1999241876 EMBASE  
TITLE: Cloning and heterologous expression of a cDNA encoding **1-deoxy-D-xylulose-5-phosphate reductoisomerase** of *Arabidopsis thaliana*.  
AUTHOR: Schwender J.; Muller C.; Zeidler J.; Lichtenthaler H.K.  
CORPORATE SOURCE: H.K. Lichtenthaler, Botanisches Institut, Universitat Karlsruhe, D-76128 Karlsruhe, Germany.  
hartmut.lichtenthaler@bio-geo.uni-karlsruhe.de

SOURCE: FEBS Letters, (1999) 455/1-2 (140-144).  
Refs: 22  
ISSN: 0014-5793 CODEN: FEBLAL  
PUBLISHER IDENT.: S 0014-5793 (99) 00849-2  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Various plant isoprenoids are synthesized via the non-mevalonate pathway of isopentenyl diphosphate formation. In this pathway, 1-deoxy-D-xylulose 5-phosphate (DOXP), the first intermediate, is transformed to 2-C-methyl-D-erythritol 4-phosphate (MEP) by an enzyme which was recently cloned from *Escherichia coli*. In order to find a plant homologue of this 1-deoxy-D-xylulose 5-phosphate reductoisomerase (DXR) we cloned a cDNA fragment from *Arabidopsis thaliana* which has high homology to the *E. coli* DXR. By expression of this fragment in *E. coli* we could demonstrate that it encodes a protein which transforms DOXP to MEP. The antibiotic fosmidomycin specifically inhibits this DXR enzyme activity. Copyright (C) 1999 Federation of European Biochemical Societies.

L5 ANSWER 10 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 2

ACCESSION NUMBER: 1998305569 EMBASE  
TITLE: A 1-deoxy-D-xylulose 5-phosphate reductoisomerase catalyzing the formation of 2-C-methyl-D-erythritol 4-phosphate in an alternative nonmevalonate pathway for terpenoid biosynthesis.

AUTHOR: Takahashi S.; Kuzuyama T.; Watanabe H.; Seto H.  
CORPORATE SOURCE: H. Seto, Inst. of Molec./Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo 113-0032, Japan.  
c00402@simail.nc.jp

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (18 Aug 1998) 95/17 (9879-9884).  
Refs: 38

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
029 Clinical Biochemistry

LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Several eubacteria including *Escherichia coli* use an alternative nonmevalonate pathway for the biosynthesis of isopentenyl diphosphate instead of the ubiquitous mevalonate pathway. In the alternative pathway, 2-C-methyl-D-erythritol or its 4-phosphate, which is proposed to be formed from 1-deoxy-D-xylulose 5-phosphate via intramolecular rearrangement followed by reduction process, is one of the biosynthetic precursors of isopentenyl diphosphate. To clone the gene(s) responsible for synthesis of 2-C-methyl-D-erythritol 4-phosphate, we prepared and selected *E. coli* mutants with an obligatory requirement for 2-C-methylerythritol for growth and survival. All the DNA fragments that complemented the defect in synthesizing 2-C-methyl-D-erythritol 4-phosphate of these mutants contained the *yaeM* gene, which is located at 4.2 min on the chromosomal map of *E. coli*. The gene product showed significant homologies to hypothetical proteins with unknown functions present in *Haemophilus influenzae*, *Synechocystis* sp. PCC6803, *Mycobacterium tuberculosis*, *Helicobacter pylori*, and *Bacillus subtilis*. The purified recombinant *yaeM* gene product was overexpressed in *E. coli*.

and found to catalyze the formation of **2-C-methyl-D-erythritol 4-phosphate** from 1-deoxy-D-xylulose 5-phosphate in the presence of NADPH. Replacement of NADPH with NADH decreased the reaction rate to about 1% of the original rate. The enzyme required Mn<sup>2+</sup>, Co<sup>2+</sup>, or Mg<sup>2+</sup> as well. These data clearly show that the *yaeM* gene encodes an enzyme, designated **1-deoxy-D-xylulose 5-phosphate reductoisomerase**, that synthesizes **2-C-methyl-D-erythritol 4-phosphate** from 1-deoxy-D-xylulose 5-phosphate, in a single step by intramolecular rearrangement and reduction and that this gene is responsible for terpenoid biosynthesis in *E. coli*.

=> d his

(FILE 'HOME' ENTERED AT 11:32:03 ON 13 JAN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHDS, SCISEARCH' ENTERED AT 11:33:02 ON 13 JAN 2004

L1 297 S 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE  
L2 162 S L1 AND ISOPRENOID  
L3 26 S L2 AND (DNA OR NUCLEIC ACID OR RNA)  
L4 12 S L3 AND 2-C METHYL-D-ERYTHRITOL 4-PHOSPHATE  
L5 10 DUP REM L4 (2 DUPLICATES REMOVED)  
L6 1 S L5 AND 1990-1998/PY

=> dup rem 13

PROCESSING COMPLETED FOR L3

L7 20 DUP REM L3 (6 DUPLICATES REMOVED)

=> s 17 and 1993-1998/py

L8 1 L7 AND 1993-1998/PY

=> d 18

L8 ANSWER 1 OF 1 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 1998305569 EMBASE

TI A **1-deoxy-D-xylulose 5-phosphate reductoisomerase** catalyzing the formation of 2-C-methyl-D-erythritol 4-phosphate in an alternative nonmevalonate pathway for terpenoid biosynthesis.

AU Takahashi S.; Kuzuyama T.; Watanabe H.; Seto H.

CS H. Seto, Inst. of Molec./Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo 113-0032, Japan. c00402@simail.nc.jp

SO Proceedings of the National Academy of Sciences of the United States of America, (18 Aug 1998) 95/17 (9879-9884).

Refs: 38

ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 004 Microbiology

029 Clinical Biochemistry

LA English

SL English

=> s 1-deoxy-D-xylulose 5 phosphate reductoisomerase and *e. coli*

L9 69 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE AND *E. COLI*

=> dup rem 19

PROCESSING COMPLETED FOR L9

L10 38 DUP REM L9 (31 DUPLICATES REMOVED)

=> focus l10  
PROCESSING COMPLETED FOR L10  
L11 38 FOCUS L10 1-

=> d 111 1-5 ibib ab

L11 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:780314 CAPLUS  
DOCUMENT NUMBER: 135:340826  
TITLE: Method for the determination of 1-  
deoxy-D-xylulose 5  
-phosphate reductoisomerase in  
microorganisms and cell cultures  
INVENTOR(S): Bacher, Adelbert; Eisenreich, Wolfgang; Fellermeier,  
Monika; Hecht, Stefan; Herz, Stefan; Rohdich, Felix;  
Wungsintawekul, Juraithip; Zenk, Meinhart H.  
PATENT ASSIGNEE(S): Germany  
SOURCE: Ger. Offen., 8 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10018368	A1	20011025	DE 2000-10018368	20000413

PRIORITY APPLN. INFO.: DE 2000-10018368 20000413  
AB The invention concerns an assay for the detn. of 1-deoxy  
-D-xylulose 5-phosphate  
reductoisomerase in microorganisms and plant cell cultures by  
using 1-deoxy-D-xylulose as substrate and a phosphorylation agent in the  
presence of a magnesium salt, sodium fluoride and glutathione. 1  
-Deoxy-D-xylulose 5-  
phosphate reductoisomerase is detd. in genetically  
engineered *E.coli*; radiolabeled substrate can be used.  
Thus a reagent contained 50 mM Tris-HCl pH 7.4, 40 mM MgCl<sub>2</sub>, 40 mM ATP, 20  
mM glutathione, 20 mM NaF, and 3.5 .mu.M [1,2-14C]1-deoxy-D-xylulose  
(24000 dpm) in 50 .mu.L including the sample. After incubation at  
37.degree.C for 1 h paper chromatog. was performed; Rf values were detd.  
with a radioactivity reader.

L11 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2000:772741 CAPLUS  
DOCUMENT NUMBER: 133:330553  
TITLE: Arabidopsis 1-deoxy-D-  
xylulose-5-phosphate  
reductoisomerase cDNA and transgenic plants  
with enhanced tocopherol content  
INVENTOR(S): Lichtenthaler, Hartmut; Schwender, Jorg; Reindl,  
Andreas; Herbers, Karin  
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000065036	A2	20001102	WO 2000-EP3465	20000417
WO 2000065036	A3	20010419		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,

ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,  
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,  
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
DE 19918949 A1 20001123 DE 1999-19918949 19990427  
EP 1180149 A2 20020220 EP 2000-922642 20000417  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: DE 1999-19918949 A 19990427  
WO 2000-EP3465 W 20000417

AB The invention relates to a method for producing plants contg. increased quantities of tocopherols, vitamin K, carotenoids, chlorophylls and polyterpenes by overexpression of a **1-deoxy-D-xylulose-5-phosphate reductoisomerase** (DXPRI) gene. Thus, the DXPRI cDNA of *Arabidopsis thaliana* was cloned, sequenced, and expressed in **E. coli**, tobacco, and *Brassica napus*. The .alpha.-tocopherol levels of the transgenic plants were increased.

L11 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1998:358885 CAPLUS  
DOCUMENT NUMBER: 129:149156  
TITLE: Direct formation of 2-C-methyl-D-erythritol 4-phosphate from 1-deoxy-D-xylulose 5-phosphate by **1-deoxy-D-xylulose 5-phosphate reductoisomerase**, a new enzyme in the non-mevalonate pathway to isopentenyl diphosphate  
AUTHOR(S): Kuzuyama, Tomohisa; Takahashi, Shunji; Watanabe, Hiroyuki; Seto, Haruo  
CORPORATE SOURCE: Institute of Molecular and Cellular Biosciences, University of Tokyo, Tokyo, 113-0032, Japan  
SOURCE: Tetrahedron Letters (1998), 39(25), 4509-4512  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB 1-Deoxy-D-xylulose 5-phosphate is biotransformed to 2-C-methyl-D-erythritol 4-phosphate in a single step in the presence of NADPH by a new recombinant enzyme named **1-deoxy-D-xylulose 5-phosphate reductoisomerase** purified from *Escherichia coli*.  
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 38 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2000:95738 BIOSIS  
DOCUMENT NUMBER: PREV200000095738  
TITLE: Biosynthesis of terpenoids: **1-Deoxy-D-xylulose-5-phosphate reductoisomerase** from *Escherichia coli* is a class B dehydrogenase.  
AUTHOR(S): Radykewicz, Tanja; Rohdich, Felix; Wungsintaweekul, Juraithip; Herz, Stefan; Kis, Klaus; Eisenreich, Wolfgang; Bacher, Adelbert; Zenk, Meinhart H.; Arigoni, Duilio [Reprint author]  
CORPORATE SOURCE: Laboratorium fur Organische Chemie, ETH Zurich, Universitatsstr. 16, CH-8092, Zurich, Switzerland  
SOURCE: FEBS Letters, (Jan. 14, 1999) Vol. 464, No. 2-3, pp. 157-160. print.  
CODEN: FEBLAL. ISSN: 0014-5793.  
DOCUMENT TYPE: Article

LANGUAGE: English  
ENTRY DATE: Entered STN: 15 Mar 2000  
Last Updated on STN: 3 Jan 2002

AB 1-Deoxy-D-xylulose-5-phosphate is converted into 2-C-methyl-D-erythritol-4-phosphate by the catalytic action of **1-deoxy-D-xylulose-5-phosphate reductoisomerase** (Dxr protein) using NADPH as cofactor. The stereochemical features of this reaction were investigated in *in vitro* experiments with the recombinant Dxr protein of *Escherichia coli* using (4R)- or (4S)-(4-2H1)NADPH as coenzyme. The enzymatically formed 2-C-methyl-D-erythritol-4-phosphate was isolated and converted into 1,2:3,4-di-O-isopropylidene-2-C-methyl-D-erythritol; NMR spectroscopic investigation of this derivative indicated that only (4S)-(4-2H1)NADPH affords 2-C-methyl-D-erythritol-4-phosphate labelled exclusively in the H<sub>4</sub> position of C-1. Stereospecific transfer of HSi from C-4 of the cofactor identifies the Dxr protein of *E. coli* as a class B dehydrogenase.

L11 ANSWER 5 OF 38 MEDLINE on STN  
ACCESSION NUMBER: 1998374274 MEDLINE  
DOCUMENT NUMBER: 98374274 PubMed ID: 9707569  
TITLE: **A 1-deoxy-D-xylulose-5-phosphate reductoisomerase**  
catalyzing the formation of 2-C-methyl-D-erythritol-4-phosphate in an alternative nonmevalonate pathway for terpenoid biosynthesis.  
AUTHOR: Takahashi S; Kuzuyama T; Watanabe H; Seto H  
CORPORATE SOURCE: Institute of Molecular and Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo 113-0032, Japan.  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Aug 18) 95 (17) 9879-84.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AB013300  
ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 19980925  
Last Updated on STN: 20030124  
Entered Medline: 19980917

AB Several eubacteria including *Escherichia coli* use an alternative nonmevalonate pathway for the biosynthesis of isopentenyl diphosphate instead of the ubiquitous mevalonate pathway. In the alternative pathway, 2-C-methyl-D-erythritol or its 4-phosphate, which is proposed to be formed from 1-deoxy-D-xylulose 5-phosphate via intramolecular rearrangement followed by reduction process, is one of the biosynthetic precursors of isopentenyl diphosphate. To clone the gene(s) responsible for synthesis of 2-C-methyl-D-erythritol 4-phosphate, we prepared and selected *E. coli* mutants with an obligatory requirement for 2-C-methylerythritol for growth and survival. All the DNA fragments that complemented the defect in synthesizing 2-C-methyl-D-erythritol 4-phosphate of these mutants contained the *yaeM* gene, which is located at 4.2 min on the chromosomal map of *E. coli*. The gene product showed significant homologies to hypothetical proteins with unknown functions present in *Haemophilus influenzae*, *Synechocystis* sp. PCC6803, *Mycobacterium tuberculosis*, *Helicobacter pylori*, and *Bacillus subtilis*. The purified recombinant *yaeM* gene product was overexpressed in *E. coli* and found to catalyze the formation of 2-C-methyl-D-erythritol 4-phosphate from 1-deoxy-D-xylulose 5-phosphate in the presence of NADPH. Replacement of NADPH with NADH decreased the reaction rate to about 1% of the original rate. The enzyme required Mn<sup>2+</sup>, Co<sup>2+</sup>, or Mg<sup>2+</sup> as well. These data clearly show that the *yaeM* gene encodes an enzyme, designated **1-deoxy-D-xylulose 5-phosphate reductoisomerase**

, that synthesizes 2-C-methyl-D-erythritol 4-phosphate from 1-deoxy-D-xylulose 5-phosphate, in a single step by intramolecular rearrangement and reduction and that this gene is responsible for terpenoid biosynthesis in *E. coli*.

=> d 111 6-10 ibib ab

L11 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1999:673053 CAPLUS  
DOCUMENT NUMBER: 131:309853  
TITLE: Process for producing isoprenoid compounds by transgenic microorganisms and method for detecting compounds having antibacterial or herbicidal activity  
INVENTOR(S): Miyake, Koichiro; Hashimoto, Shinichi; Motoyama, Hiroaki; Ozaki, Akio; Seto, Haruo; Kuzuyama, Tomohisa; Takahashi, Shunji  
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 145 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953071	A1	19991021	WO 1999-JP1987	19990414
W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2000300256	A2	20001031	JP 1999-104589	19990412
JP 2000300257	A2	20001031	JP 1999-104590	19990412
CA 2325798	AA	19991021	CA 1999-2325798	19990414
AU 9931699	A1	19991101	AU 1999-31699	19990414
EP 1072683	A1	20010131	EP 1999-913662	19990414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			JP 1998-103101	A 19980414
			JP 1998-221910	A 19980805
			JP 1999-35739	A 19990215
			WO 1999-JP1987	W 19990414

AB Disclosed is a method for the prodn. of isoprenoid compds. by cultivating transgenic prokaryotes that have been transformed with the gene for (1) 1-deoxy-D-xylulose 5-phosphate synthetase; (2) farnesyl pyrophosphate synthetase; (3) exodeoxyribo-nuclease; (4) a defined protein; and/or (5) 1-deoxy-D-xylulose 5-phosphate reductoisomerase. The transgenic prokaryotes are selected from *Escherichia*, *Rhodobacter*, or *Erwinia*. The isoprenoid compds. are useful for (1) the treatment of heart diseases or osteoporosis, hemostasis, prevention of cancer, immunopotentiation, etc. and (2) the prepn. of health foods, antifouling coatings, etc. A method for screening compds. for their antibacterial or herbicidal activity or herbicidal activity by detecting their inhibitory activity against the enzymes assocd. with the non-mevalonate pathway is also claimed. Isolation of the genes assocd. with the biosynthesis of isoprenoid compds. from *Escherichia coli* strain XL1-Blue and use of the genes to improve the yield of CoQ8 by transgenic *E. coli* DH5. $\alpha$  were shown. The *Rhodobacter sphaeroides* counterparts of gene DKS were also provided.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 38 MEDLINE on STN  
ACCESSION NUMBER: 2000123893 MEDLINE  
DOCUMENT NUMBER: 20123893 PubMed ID: 10631325  
TITLE: Biosynthesis of terpenoids: 1-deoxy-D-xylulose-5-phosphate  
reductoisomerase from *Escherichia coli* is a class B dehydrogenase.  
AUTHOR: Radykewicz T; Rohdich F; Wungsintaweekul J; Herz S; Kis K; Eisenreich W; Bacher A; Zenk M H; Arigoni D  
CORPORATE SOURCE: Lehrstuhl fur Organische Chemie und Biochemie, Technische Universitat Munchen, Lichtenbergstr. 4, D-85747, Garching, Germany.  
SOURCE: FEBS LETTERS, (2000 Jan 14) 465 (2-3) 157-60.  
Journal code: 0155157. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200002  
ENTRY DATE: Entered STN: 20000309  
Last Updated on STN: 20000309  
Entered Medline: 20000218

AB 1-Deoxy-D-xylulose-5-phosphate is converted into 2-C-methyl-D-erythritol-4-phosphate by the catalytic action of 1-deoxy-D-xylulose-5-phosphate (Dxr protein) using NADPH as cofactor. The stereochemical features of this reaction were investigated in *in vitro* experiments with the recombinant Dxr protein of *Escherichia coli* using (4R)- or (4S)-[4-(2)H(1)]NADPH as coenzyme. The enzymatically formed 2-C-methyl-D-erythritol-4-phosphate was isolated and converted into 1,2:3,4-di-O-isopropylidene-2-C-methyl-D-erythritol; NMR spectroscopic investigation of this derivative indicated that only (4S)-[4-(2)H(1)]NADPH affords 2-C-methyl-D-erythritol-4-phosphate labelled exclusively in the H(Re) position of C-1. Stereospecific transfer of H(Si) from C-4 of the cofactor identifies the Dxr protein of *E. coli* as a class B dehydrogenase.

L11 ANSWER 8 OF 38 MEDLINE on STN  
ACCESSION NUMBER: 1999355442 MEDLINE  
DOCUMENT NUMBER: 99355442 PubMed ID: 10428488  
TITLE: Cloning and heterologous expression of a cDNA encoding 1-deoxy-D-xylulose-5-phosphate reductoisomerase of *Arabidopsis thaliana*.  
AUTHOR: Schwender J; Muller C; Zeidler J; Lichtenthaler H K  
CORPORATE SOURCE: Botanisches Institut, Universitat Karlsruhe, Germany.  
SOURCE: FEBS LETTERS, (1999 Jul 16) 455 (1-2) 140-4.  
Journal code: 0155157. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AJ242588  
ENTRY MONTH: 199908  
ENTRY DATE: Entered STN: 19990827  
Last Updated on STN: 19990827  
Entered Medline: 19990816

AB Various plant isoprenoids are synthesized via the non-mevalonate pathway of isopentenyl diphosphate formation. In this pathway, 1-deoxy-D-xylulose 5-phosphate (DOXP), the first intermediate, is transformed to 2-C-methyl-D-erythritol 4-phosphate (MEP) by an enzyme which was recently cloned from *Escherichia coli*. In order to find a plant homologue of this 1-deoxy-D-xylulose 5-phosphate reductoisomerase (DXR) we cloned a cDNA fragment from *Arabidopsis thaliana* which has high homology to the

**E. coli** DXR. By expression of this fragment in **E. coli** we could demonstrate that it encodes a protein which transforms DOXP to MEP. The antibiotic fosmidomycin specifically inhibits this DXR enzyme activity.

L11 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:23430 CAPLUS  
DOCUMENT NUMBER: 138:69471  
TITLE: Docking a ligand to a macromolecule by a combination of NMR measurements and computational modeling, and applications to protein-ligand interactions and structure-based drug design  
INVENTOR(S): Sem, Daniel S.; Pellecchia, Maurizio  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 32 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003008326	A1	20030109	US 2002-158770	20020530
PRIORITY APPLN. INFO.:			US 2001-294675P	P 20010530

AB The present invention relates generally to interactions between macromols. and ligands and more specifically to NMR methods for detg. structure-related properties of a ligand when bound to a macromol. The invention provides a method for detg. a structure model for a test ligand bound to a macromol. binding site by a combination of NMR measurements and computational modeling. Structural constraints for the test ligand are derived from spectroscopic signals arising from interactions between the test ligand and macromol. The structure constraints are used as constraints in docking a structure model of the ligand to a structure model of the macromol., or as constraints in overlaying a structure model of the test ligand on the known structure for a ref. ligand that binds to the macromol. The invention further provides a method for detg. a structure model for a macromol. bound to a ligand. Structural constraints derived from spectroscopically obsd. interactions of the macromol. and a ref. ligand are used to guide mol. modeling or to evaluate the results of a mol. modeling simulation of the macromol. An advantage of the invention is that a structure model of a test ligand bound to the macromol. can be obtained at sufficient resoln. to assist in structure-based design of a biol. active agent or drug without the requirement for a complete detn. of the structure of the macromol.-test ligand complex. Examples include: docking of a furoic acid-based inhibitor into the NADH binding site of **E. coli** dihydridopicolinate reductase (DHPR); overlay of a furoic acid-based inhibitor onto DHPR-bound NADH; validation of a binding site homol. model for **1-deoxy-D-xylulose-5-phosphate reductoisomerase** (DOXPR), and identifying a residue of DOXPR that is at an interface between ligand binding sites.

L11 ANSWER 10 OF 38 MEDLINE on STN  
ACCESSION NUMBER: 2000387137 MEDLINE  
DOCUMENT NUMBER: 20347905 PubMed ID: 10787409  
TITLE: Characterization of **1-deoxy-D-xylulose 5-phosphate reductoisomerase**, an enzyme involved in isopentenyl diphosphate biosynthesis, and identification of its catalytic amino acid residues.  
AUTHOR: Kuzuyama T; Takahashi S; Takagi M; Seto H  
CORPORATE SOURCE: Institute of Molecular and Cellular Biosciences, University of Tokyo, Yayoi, Bunkyo-ku, Tokyo 113-0032, Japan.  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 30) 275 (26)

19928-32.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200008  
ENTRY DATE: Entered STN: 20000818  
Last Updated on STN: 20000818  
Entered Medline: 20000810

AB 1-Deoxy-d-xylulose 5-phosphate (DXP) reductoisomerase, which simultaneously catalyzes the intramolecular rearrangement and reduction of DXP to form 2-C-methyl-d-erythritol 4-phosphate, constitutes a key enzyme of an alternative mevalonate-independent pathway for isopentenyl diphosphate biosynthesis. The dxr gene encoding this enzyme from *Escherichia coli* was overexpressed as a histidine-tagged protein and characterized in detail. DNA sequencing analysis of the dxr genes from 10 *E. coli* dxr-deficient mutants revealed base substitution mutations at four points: two nonsense mutations and two amino acid substitutions (Gly(14) to Asp(14) and Glu(231) to Lys(231)). Diethyl pyrocarbonate treatment inactivated DXP reductoisomerase, and subsequent hydroxylamine treatment restored the activity of the diethyl pyrocarbonate-treated enzyme. To characterize these defects, we overexpressed the mutant enzymes G14D, E231K, H153Q, H209Q, and H257Q. All of these mutant enzymes except for G14D were obtained as soluble proteins. Although the purified enzyme E231K had wild-type K(m) values for DXP and NADPH, the mutant enzyme had less than a 0.24% wild-type k(cat) value. K(m) values of H153Q, H209Q, and H257Q for DXP increased to 3.5-, 7.6-, and 19-fold the wild-type value, respectively. These results indicate that Glu(231) of *E. coli* DXP reductoisomerase plays an important role(s) in the conversion of DXP to 2-C-methyl-d-erythritol 4-phosphate, and that His(153), His(209), and His(257), in part, associate with DXP binding in the enzyme molecule.

=> d his

(FILE 'HOME' ENTERED AT 11:32:03 ON 13 JAN 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, BIOTECHDS, SCISEARCH' ENTERED AT 11:33:02 ON 13 JAN 2004

L1 297 S 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE  
L2 162 S L1 AND ISOPRENOID  
L3 26 S L2 AND (DNA OR NUCLEIC ACID OR RNA)  
L4 12 S L3 AND 2-C METHYL-D-ERYTHRITOL 4-PHOSPHATE  
L5 10 DUP REM L4 (2 DUPLICATES REMOVED)  
L6 1 S L5 AND 1990-1998/PY  
L7 20 DUP REM L3 (6 DUPLICATES REMOVED)  
L8 1 S L7 AND 1993-1998/PY  
L9 69 S 1-DEOXY-D-XYLULOSE 5 PHOSPHATE REDUCTOISOMERASE AND E. COLI  
L10 38 DUP REM L9 (31 DUPLICATES REMOVED)  
L11 38 FOCUS L10 1-

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	120.94	121.36
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.93	-6.93

STN INTERNATIONAL LOGOFF AT 11:44:57 ON 13 JAN 2004